

Remarks

In the Office Action, the Examiner noted that claims 1 to 4 are pending in the application; and that claims 1 to 4 are rejected. By this amendment, claims 1 to 4 have been cancelled without prejudice or disclaimer of the subject matter contained therein. New claims 5 to 8 are presented, which are substantially same as original claims 1-4 but have been re-written to place them in condition for allowance by overcoming the outstanding rejections. Thus, claims 5 to 8 are pending in the application. No new subject matter has been inserted through these amendments. All of the amendments are fully supported by the specification. The Examiner's rejections are respectfully traversed below.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-4 stand rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a process which is wholly in operable.

As noted, claims 1-4 have been canceled without prejudice and new claims 5-8 have been presented by way of this amendment. Claim 5 is substantially same as claim 1 but has been re-written to provide all of the steps involved so as to make claim 5 operable. Specifically, claim 5 recites collection of a plasma sample or an urine sample from a patient who has been administered the drug and isolating the sulfate conjugate of said drug from a chromatographic techniques after any needed treatment of the sample. Support for such detailed steps can be found in the specification at page 17, lines 9 to 17. Please further note that claims 6-8 are same as claims 2-4 but claim 8 specifically recites high performance liquid chromatography. In view of the foregoing, it is respectfully submitted that new claims 5-8 fully satisfy the requirements of 35 USC 112, 2nd paragraph. Accordingly, withdrawal of rejection as to claims 1-4 is respectfully requested.

Rejection Under 35 U.S.C. § 101

Claims 1-4 stand rejected under 35 U.S.C. 101 because the Examiner alleges that the claims are wholly inoperable.

However, as noted above and the arguments as presented under 35 USC 112, 2nd paragraph rejection, it is respectfully submitted that the new claims 5-8 are fully operable. In view of the foregoing, it is submitted that new claims 5-8 fully satisfy the requirements of 35 USC 101. Accordingly, withdrawal of rejection as to claims 1-4 is respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

Claims 1-4 stand rejected under 35 USC 103(a) as being unpatentable over Scott and Heath (J. Am. Soc. Mass Spect., 1997, v. 8, 371-379) in view of Tippins (Am. Lab., 1987, v. 19, 107-114) or Wiltshire (302-341, 2000)

In particular, Scott and Heath discloses a method based on liquid chromatography for identifying and quantifying (+)- α -(2,3-dimethoxyphenyl)-1-[2-(4-fluorophenyl)ethyl]-4-piperidinemethanol and its desmethyl metabolite from animal samples such as in rat brain. Tippins reviews a state of the art in identification and quantification of a variety of endogenous compounds by solid-phase extraction techniques and clearly admits that it is an emerging field yet involves difficult to extract materials. As concluded therein:

“For several years, solid-phase extraction has been used for the selective extraction of pharmaceutical compounds and for therapeutic drug monitoring. Recently, this powerful sample preparation technique has been *utilized to solve the difficult extraction problems encountered for preparative purifications and when naturally occurring levels of endogenous compounds are measured.* The choice of nonpolar, polar, ion-exchange, or covalent extraction sorbents provides the analyst with the selectivity needed to get clean extracts with high recoveries.” (emphasis added)

Finally, Wiltshire is a review article providing strategies for isolating and identifying a variety of metabolites. It is clear from both of these articles and from above excerpt that these separation techniques are still complex and each case may involve a different technique. More importantly, none of these articles including Scott and Heath or Tippins or Wiltshire teaches or suggests isolation of sulfate conjugates from a biological source as presently taught in the instant invention and specifically claimed in claims 5-8. Thus it is submitted that claims 5-8 are

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patentably distinguishable from Scott and Heath in view of Tippins or Wiltshire. Accordingly, withdrawal of rejection as to claims 1-4 is respectfully requested.

Double Patenting Rejection

Claims 1-4 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 35-42 of U.S. Patent No. 6,465,490.

Applicants submit herewith a terminal disclaimer obviating this rejection. In addition, a statement accompanying the terminal disclaimer is also enclosed herewith. The terminal disclaimer clearly states that the assignee of record, Aventis Pharmaceuticals Inc., is the sole owner with 100 percent interest in the instant application as well as the above noted U. S. Patent No. 6,465,490. Thus, withdrawal of rejection as to claims 1-4 is respectfully requested.

Conclusions

In view of the above Remarks, it is respectfully submitted that claims 5 to 8 are now in condition for allowance and the early issuance of this case is respectfully requested. In the event the Examiner wishes to contact the undersigned regarding any matter, please call (collect if necessary) the telephone number listed below.

Applicants believe there are no fees due for this Rule 111 Amendment. However, if the Examiner deems that fees are due, please charge these fees to Deposit Account No. **18-1982** for sanofi-aventis U.S. LLC, Bridgewater, NJ. Please credit any overpayment to Deposit Account No. **18-1982**.

Respectfully submitted,

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